IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Serial No.:	10/761899	Group Art Unit:	3762
Filed:	January 21, 2004	Docket No.:	14450.0006US01
Title:	METHOD AND SYSTEM FOR THE DETERMINATION OF BLOOD CHARACTERISTICS		

CERTIFICATE UNDER 37 CFR 1.8:
I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail, with sufficient postage, in an envelope addressed to: Commissioner for Patents, Mail Stop Amendment, P.O. Box 1450, Alexandria, VA 22313-1450 on January 5, 2005.

By: _____
Name: Natalie C. Berland

SUBMISSION OF PRIORITY DOCUMENT(S)

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

Applicants enclose herewith one certified copy of an Australian Patent application, Serial No. 2003900261, filed January 22, 2003, the right of priority of which is claimed under 35 U.S.C. § 119.

Respectfully submitted,

23552
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144 P.D. 6006-US01

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Patent Office
Canberra

I, JULIE BILLINGSLEY, TEAM LEADER EXAMINATION SUPPORT AND SALES hereby certify that annexed is a true copy of the Provisional specification in connection with Application No. 2003900261 for a patent by USCOM PTY LTD as filed on 22 January 2003.

WITNESS my hand this
Fourteenth day of January 2004

J. Billingsley

JULIE BILLINGSLEY
TEAM LEADER EXAMINATION
SUPPORT AND SALES

AUSTRALIA

PATENTS ACT 1990

PROVISIONAL SPECIFICATION

FOR THE INVENTION ENTITLED:-

"METHOD AND SYSTEM FOR THE DETERMINATION OF BLOOD CHARACTERISTICS"

The invention is described in the following statement:-

FIELD OF THE INVENTION

The present invention relates to the measurement of blood flow in the body and, in particular, to the measurement of cardiac output from the heart.

BACKGROUND OF THE INVENTION

Cardiac output and measurement of cardiac dimensions and haemodynamics are very important indicators in measuring health or detecting disease. The cardiac output, the volume of blood ejected by the heart per minute, is an essential measure of cardiac health.

Unfortunately, it is often difficult to measure actual cardiac output. Whilst normal fluid flow outputs consist of a flow velocity times a cross section area, it is often difficult to accurately measure the cross sectional area of cardiac vessels. Hence, there is often a large degree of error associated with actual cardiac measurements.

SUMMARY OF THE INVENTION

It is an object of the present invention to provide for improved or alternative measures of cardiac output.

In accordance with a first aspect of the present invention, there is provided a method of determining the cardiac output of a patient, the method comprising the steps of: (a) measuring the patients height; (b) measuring the velocity time integral or stroke distance of blood flowing from the heart of the patient, (c) utilising the two measurements in step (a) and (b) to determine the cardiac output of the patient.

Preferably the method also includes the step of measuring the correlation between the patient's height and cross sectional area of a cardiac valve of a population of individuals and utilising the correlation in step (c) to determine the cardiac output of the patient. The population can be selected having similar body characteristics to the patient.

The step (c) can comprise utilising the formula substantially of the form: aortic annular diameter = 0.010 x height (cms) + 0.25cm to determining the diameter of the aortic annular and then determining a cross sectional.

The step (c) can comprise utilising the formula substantially of the form: pulmonary annular diameter = 0.0106 x height (cms) + 0.265cm to determine the diameter of the pulmonary valve and then determining a cross sectional area.

BRIEF DESCRIPTION OF THE DRAWINGS

The preferred embodiments of the present invention will now be described with reference to the accompanying drawings in which:

Fig. 1 and Fig. 2 illustrate screen dumps of CW ultrasound type devices.

DESCRIPTION OF PREFERRED AND OTHER EMBODIMENTS

In the preferred embodiment, a new method is provided for measurement of cardiac output through the utilisation of correlations between height measurements and integrated transvalvular haemodynamics.

Recently, in PCT application No. PCT/AU99/ 00507 entitled "Ultrasonic Cardiac Output Monitor" the contents of which are hereby incorporated by cross reference, a system was proposed for the continuous wave Doppler direct measurement of transvalvular cardiac flows. Such a system can readily be adapted for use with the preferred embodiment of the present invention to measure flow outputs.

Turning to Fig 1, there is illustrated a screen dump from an ultrasonic transducer device being placed in accordance with the teaching of the aforementioned application so as to measure transvalvular flows. In Fig 2, there is illustrated an analysis of the image of Fig 1. In such a system, cardiac output (CO) can be calculated by measurement of the Doppler spectral flow profile of the image of Fig. 1 to determine the

area under the curve or the velocity time integral (vti) or stroke distance – the distance a single red blood cell travels per beat. In Fig. 2, there is illustrated the vti 10 which is an "area under the curve" measurement. Further, the heart rate can be determining from the spectral flow profile as the time between peaks e.g. 11, 12.

From a measurement of the cross sectional area of the flow (XSA), it is possible to determine the stroke volume (SV) by multiplying the vti so that SV = vti x XSA. SV is the volume of blood ejected by the heart per beat in cm^3. CO is a function of SV and heart rate (HR), or the volume per beat times the number of beats per minute, so CO = SV x HR in litres per minute.

The values for these formulae can be derived from direct measurement of the Doppler flow profile of Fig. 1 and Fig. 2, with the exception of the flow cross sectional area.

One possibility for measuring the flow cross-sectional area is to measure the flow diameter using two-dimensional ultrasound, and calculating the XSA using πr^2. However, normal values for flow diameters obtained are in the order of 1.5 to 2.5cm. The resolution of 2D B-Mode ultrasound at 3Mhz is approximately 1mm or 5%. This 5% linear error is the best possible result and, if 95% confidence intervals define sensitivity and equal two standard deviations then the error is approximately 10%. If this error is squared when applied to the πr^2 formula to determine XSA, the resulting potential error in measurement of the cardiac output is approximately 21%.

It will be noted that the error associated with measurement of the Doppler functions alone for application of these haemodynamics equations is less than 5%. The figures for sensitivity of Doppler echo detection of changes in CO are reflected in clinical data. In the preferred embodiment, a more accurate method of measuring flow diameter is utilised to provide an increase in the sensitivity of Doppler ultrasound to

detection of changes in cardiac output and to thereby improve the clinical usefulness of Doppler flow measurements.

CO measurements are generally made from Doppler flow profiles across the aortic and pulmonary valves. However it is also possible to determine CO from the flow across the mitral and tricuspid valves. 'Measurement of Aortic annular diameter, the 2D measure from which XSA is derived can generally be performed with reasonable accuracy because the arterial walls are perpendicular to insonation in the parasternal long axis position, resulting in high levels of reflected signals. Measurement of the pulmonary annular diameter is more problematic because the vessel walls are often parallel to the ultrasound beam and reflected signal less intense. Of additional importance, the pulmonary artery is the most accessible flow signal for Doppler measurement of CO.

Recently, Nidorf et al (Nidorf SM, Picard MH, Triulzi MO, Thomas JD, Newell J, King, ME, Weyman AE. New perspectives in the assessment of cardiac chamber dimensions during development and adulthood. J Am Coll Cardiac 1992;19:983-8) in a study of 268 normal persons aged 6days to 76yrs, found that height, not gender, weight or BSA, was the best independent predictor of the cardiac linear dimensions of aortic annular diameter (r=0.96), Left atrial size (r=0.91), LVDd (r=0.94) and LV length (r=0.93). Further this study found that the heart and great vessels grow in unison and at a predictable rate after birth reaching 50% of their adult dimensions at birth, 75% at 5yrs and 90% at 12yrs. It should be further noted that height has the additional benefits of being a non-derived unit, is easily measured, and is a commonly patient informed value.

The size of the aortic annular diameter can be approximately described by regression equation as 0.010 x height (cms) + 0.25cms. If, as Nidorf found, the heart grows in unison and at a predictable rate, then the pulmonary artery annular diameter

will show constant a relationship to the aortic annulus at any age. Hence, the Cardiac Output can be predicted using the aortic annular diameter regression equation and integrated haemodynamics. As input CO equals output CO in the absence of shunt or significant regurgitation, a height referenced equation to predict the pulmonary artery annular diameter can also be utilised. This can then be applied to standard haemodynamics to determine flow XSA, SV and CO.

A measure for a population of individuals was studied and derived vti values of children and adults found in our own normal population to be: Pvti = 20.76±3.36cm and Avti = 23.38±3.38cm, with a vti PV:AV ratio of 1:1.126.

Whilst the above values have been used below, obviously other population samples could be utilised.

Now the ratio of PV:AV was found to be 1.126. As CO = OT x HR x vti, and pulmonary flow equals systemic (aortic) flow in the absence of a shunt or significant regurgitation, then

PV XSA x HR x PVvti = AV XSA x HR x AVvti

As XSA = πr^2 and AVd = (0.01 x ht + 0.25) and AVr = (0.01 x ht + 0.25)/2 then

$$(\pi \times (PVd/2)^2) \times 20.76 \times HR = (\pi \times ((0.01 \times ht + 0.25)/2)^2) \times 23.38 \times HR$$

If HR PV = HR AV then

$$(\pi \times (PVd/2)^2) \times 20.76 = (\pi \times ((0.01 \times ht + 0.25)/2)^2) \times 23.38/20.76$$

$$(\pi \times (PVd/2)^2) = (\pi \times ((0.01 \times ht + 0.25)/2)^2) \times 23.38/20.76$$

$$\pi \times (PVd/2)^2 = \pi \times ((0.01 \times ht + 0.25)/2)^2 \times 1.126/\pi$$

$$(PVd/2)^2 = ((0.01 \times ht + 0.25)/2)^2 \times 1.126$$

Taking the square root of both sides implies:

$$\sqrt{(PVd/2)^2} = \sqrt{((0.01 \times ht + 0.25)/2)^2} \times \sqrt{1.126}$$

$$PVd/2 = (0.01 \times ht + 0.25)/2 \times 1.06$$

$$PVd/2 = (0.01 \times ht + 0.25) \times 1.06/2$$

Then PV Radius = $PVd/2 = (0.01 \times ht + 0.25) \times 0.53 = 0.053 \times ht + 0.1325$

and PV diameter = $PVd/2 \times 2 = (0.01 \times ht + 0.25) \times 1.06 = 0.0106 \times ht + 0.265$

Therefore both the aortic annular and the pulmonary annular diameter can be determined from simple height measurements as

$$AVd = 0.01 \times ht + 0.25$$

and

$$PVd = 0.0106 \times ht + 0.265$$

As a result, the above formulas can be utilised to calculate the cross-sectional area of the aortic and pulmonary valves. From this calculation, the stroke volume and CO can also be determined.

The flow cross sectional area, XSA, in cm^2 is required to calculate flow volumes and can be determined from direct 2D measurements or calculated from height referenced algorithms. From the above, the XSA algorithms are:

Aortic

As $AVd = 0.010 \times ht + 0.25$

Pulmonary

As $PVd = 0.0106 \times ht + 0.265$

then PV $XSA = \pi ((0.0106 \times ht) + 0.265)./2)^2$

Stroke Volume

Stroke volume, in cm^3, is the volume of blood ejected from the heart per beat and is equal to the cross sectional area times the flow vti. Therefore:

SV AV (adult + children) $= \pi ((0.010 \times ht + 0.25)/2)^2 \times AVvti$

SV PV (adult + children) $= \pi ((0.0106 \times ht + 0.265)/2)^2 \times PVvti$

Cardiac Output

Cardiac output, in litres per minute, is the volume of blood ejected from the heart per minute and is a function of the cross sectional area, the flow vti and the heart rate.

$$\text{CO AV (adult + children)} = \pi ((0.010 \times \text{ht} + 0.25)/2)^2 \times \text{AVvti} \times \text{HR}$$

$$\text{CO PV (adult + children)} = \pi ((0.0106 \times \text{ht} + 0.265)/2)^2 \times \text{PVvti} \times \text{HR}$$

By using the above formulas, a determination of important cardiac morphologic dimensions can be made from a subject height measurement. This measurement provides an alternative to the currently practiced direct measurement of these dimensions using complex imaging. This can allow for stand alone Doppler instruments to determine accurate measures of cardiac function without the use of complex and expensive imaging devices. This results in an improved method of determining CO in echocardiographic practice.

The foregoing describes only preferred embodiments of the present invention. Modifications, obvious to those skilled in the art can be made there to without departing from the scope of the invention.

THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. A method of determining the cardiac output of a patient, the method comprising the steps of:

(a) measuring the patients height;

(b) measuring the velocity time integral or stroke distance of blood flowing from the heat of the patient; and

(c) utilising the two measurement in step (a) and step (b) to determine the cardiac output of the patient.

2. A method as claimed in claim 1 further comprising the step of measuring the correlation between the patient's height and cross sectional area of a cardiac valve of a population of individuals and utilising the correlation in step (c) to determine the cardiac output of the patient.

3. A method as claimed in claim 2 wherein said population is selected having similar body characteristics to said patient.

4. A method as claimed in claim 1 wherein said step of utilising comprises utilising the formula substantially of the form:

aortic annular diameter = 0.010 x height (cms) + 0.25cm

to determine the diameter of the aortic annular and then determining a cross sectional.

5. A method as claimed in claim 1 wherein said step of utilising comprises utilising the formula substantially of the form:

aortic annular diameter = 0.010 x height (cms) + 0.25cm

to determine the diameter of the aortic annular and then determining a cross sectional area.

6. A method as claimed in claim 1 wherein said step of utilising comprises utilising the formula substantially of the form:

pulmonary annular diameter = 0.0106 x height (cms) + 0.265cm

to determine the diameter of the pulmonary valve and then determining a cross sectional area.

7. A method of determining the cardiac output of a patient substantially as hereinbefore described with reference to the accompanying drawings.

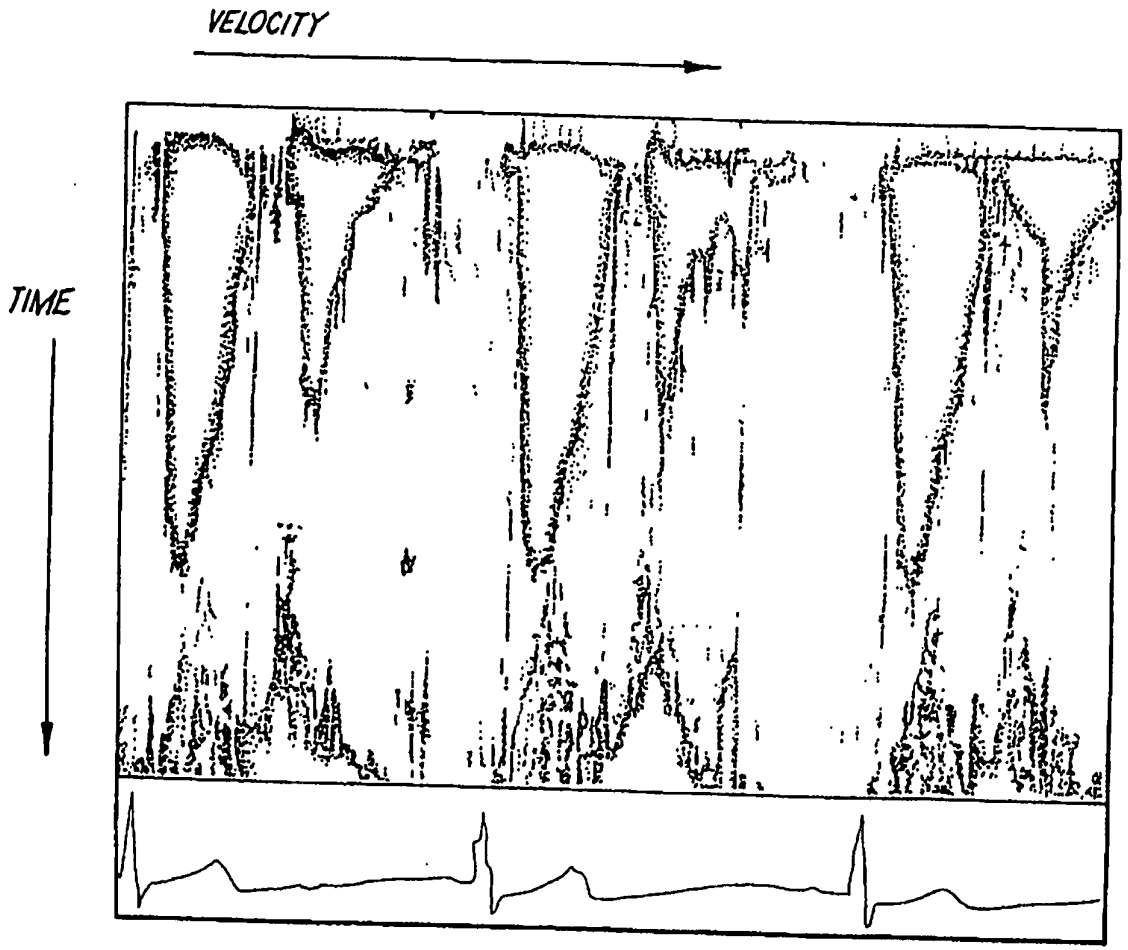

FIG. 1

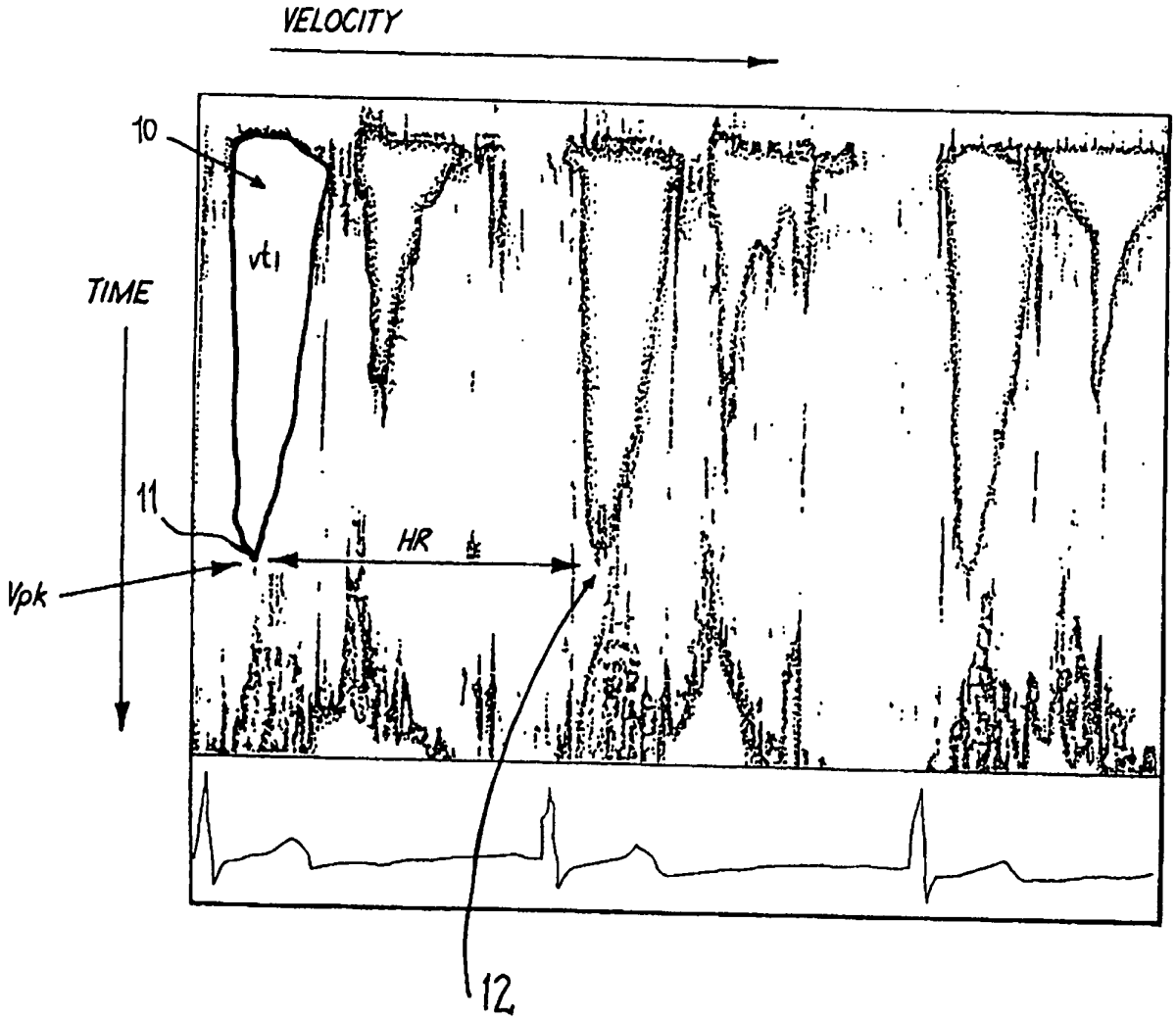

FIG. 2